U.S. DEPARTMENT OF COMMERCE Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name:	Serial Number:		
Date:	Phone:	Ar	t Unit:
Search Topic: Please write a detailed statement of terms that may have a special mean please attach a copy of the sequence			
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Date completed: 07-29- Searcher: Benery		arch Site STIC	Vendors IG
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Number of Searches: Number of Databases:		A.A. Sequence Structure	DARC/Questel

PTO-1590 (9-90)



STIC Search Report Biotech-Chem Library

STIC Database Tracking Number: 99905

To: Sarvamangala Devi

Location: CM1-7E12

Art Unit: 1645

Tuesday, July 29, 2003

Case Serial Number: 10/060521

From: Beverly Shears

Location: Biotech-Chem Library

CM1-1E05

Phone: 308-4994

beverly.shears@uspto.gov

Search Notes			
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Copyright (c) 1993 - 2003 Compugen Ltd.
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HarA protein or nucleic acid is useful in the screening/manufacture of a compound for use as a medicament for the treatment of a drug resistant infection. HarA nucleic acid is useful to identify an organism containing a harA gene. HarA protein is useful to screen for B. faecalis antibodies in blood or serum and samples from animals, or as antigens to raise antibodies, which antibodies are useful as diagnostic reagents. The identified compounds are useful in the treatment of enterococcal infections (e.g. sepsis, septic shock, bacterial endocarditis and prostatitis) as well as staphylococcal and pneumococcal infections.

The nucleic acid is useful as a hybridisation probe for RNA, cDNA and genomic DNA to isolate full-length cDNAs and genomic Clones encoding harA polypeptides and to isolate cDNA and genomic clones of other genes that have a high sequence similarity to harA gene. HarA has NTPase activity. The present sequence is the B. faecalis
                                                                                                                                                         Query Match
Best Local Similarity
Matches 498; Conser
                                                                                                                                                                                                                                    Sequence
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         The invention relates to a recombinant hygromycin A resistance (harA) polypeptide comprising a sequence which is at least 75% identical to the harA protein form Enterococcus faecalis and Bacillus subtilis. Also included are: (1) use of a hygromycin A-resistant strain of Enterococcus faecalis or Bacillus subtilis to determine whether an antibacterial agent is effective in treating organisms which exhibit harA-mediated drug resistance; (2) the nucleic acid encoding the harA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              HarA; enzyme; hygromycin A resistance; bacterial infection; sepsis; septic shock; bacterial endocarditis; prostatitis; NTPase; staphylococcal infection; pneumococcal infection.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Novel hygromycin A resistance polypeptide derived from Enterococcus faecalis and Bacillus subtilis useful for screening compounds which binds to the polypeptide, and as medicament for treating drug resistant
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Claim 12; Fig 2; 43pp; English.
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61 ILHQVDFVYFPQTVAEEQQLTYYVLQEVTSFEQWELERELTLLNVDPEVLMRPFSSLSGG
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                                                                                                                                                                                                                           Determining whether a candidate nucleotide or polypeptide encodes/functions as a multidrug resistance (MDR) efflux pump searching a database of nucleotide/polypeptide sequences for thigh identity to known MDR pumps -
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Matches 494
                                                                                                                                                                                                                                                                                                                                                                                          further identifying MDR efflux pumps that may be used as drug target increase the sensitivity of cells to antibacterial agents. Cells comprising the identified pumps may be used to screen for potential blockers or inhibitors of MDR pump function or gene expression.
                                                                                                                                                                                                                                                                                                                                                                          Sequence
                 481
                                    421
                                                       421
                                                                        361
                                                                                         361
                                                                                                            301
                                                                                                                             301
                                                                                                                                               241
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                                                                                                                                                                                   181
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                                                                                                                                                                                                                        121
                                                                                                                                                                                                                                          121
                                                                                                                                                                                                                                                                                                                                      494;
                                                                                                                                                                                                                                                             2
                                                                                                                                                                                                                                                                              13
                                                                                                                                                                                                                                                                                                                   μ
                                                                                                                                                                                                                                                                                                                                               Similarity
                                                                                                                                                                                                                                                                                              ILHQVDFVYFPQTVAEEQQLTYYVLQBVTSFEQWELERELTLLAVDPBVLWRPFSSLSGG
HDAHFMKKI TDKKI VLKS
                                  NPSGDSEGEATLAHOLTISYVRODYEDNOGTLSEFAEKNOLDYTOFLANLRKLGMERAVF
                                                                                                            SMDYQPTHHKTLLTVBELRLGYEKNMLFAPLSFSINAGEIVGITGKNGSGKKSSLIQYLLD
                                                                                                                                               EGDKYGNAKEKGSGA I FDYGA I GARAARVMKRSKH I QQRAETQLAEKBKLLKDLEY I DSL
                                                                                                                                                          EGDKYGNAKEKGSGAIFDTGAIGARAARVMKRSKHIQQRAETQLAEKEKLLKDLEYIDPL
                                                                                                                                                                                   DHILAIBKSQLTLYQGNFSIYBBQKKLRDAFBLAENBKIKKBVNRLKSTARKKABWSMNR
                                                                                                                                                                                              DHILAIEKSQLTLYQGNFSIYEBQKKLRDAFELAENEKIKKEVNRLKETARKKAEWSMNR
                                                                                                                                                                                                                                                            ILHQVDFVYFPQTVABEQQLITYYVLQEVTSFEQWKLERELTLLNVDPEVLWRPFSSLSGG
                                                                                                                                                                                                                                                                                                                                                                          498 AA;
                                                                                                                                                                                                                                                                                                                                      Conservative
                                                                                                                                                                                                                                                                                                                                              99.3%;
                                                                                                                                                                                                                                                                                                                                      2
                498
                                                                                                                                                                                                                                                                                                                                               Score 2522;
Pred. No. 5
                                                                                                                                                                                                                                                                                                                                      Mismatches
                                                                                                                                                                                                                                                                                                                                               DB 22;
                                                                                                                                                                                                                                                                                                                                         Indels
                                                                                                                                                                                                                                                                                                                                                        Length
                                                                                                                                                                                                                                                                                                                                                                                                                as drug targets
ints. Cells
                                                                                                                                                                                                                                                                                                                                                         498;
                                                                                                                                                                                                                                                                                                                                       0
                                                                                                                                                                                                                                                                                                                                         Gaps
                                                                                                                           360
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                                                                                                                                                   300
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                                                                                                                                                                                                                                                                                                                      6
                                                         480
                                                                                            420
                                                                                                               360
                                       480
                                                                          420
```

480

420

480

420 360 360 300 300

Search completed: July Job time: 99 secs 28, 2003, 15:39:59

481

498

The invention relates to determining whether a candidate nucleotide (ABA82938-ABA82971) or polypeptide (ABA87256-ABB47296) encodes/functions as a multidrug resistance (MDR) efflux pump comprising, searching a database for sequences high identity known MDR efflux pumps and then deleting/mutating an identified region of the DNA in a bacterial cell and determining whether the bacterial cell exhibits increased or decreased sensitivity to an antibacterial agent The identified pumps are useful for

Claim

10; Fig 26; 139pp; English.

```
Result
No.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Title:
Perfect score:
Sequence:
                                                                                                                                                                                                                                                                                                                                                                                                                       Database :
                                                                                                                                                                                                                                                                                                                                                                                                                                                       Post-processing: Minimum Match 75%
Maximum Match 100%
Listing first 1000 summaries
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               OM protein - protein search, using sw model
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Minimum DB seq length: 0
Maximum DB seq length: 2000000000
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Scoring table:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Searched:
matches found
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           al number of hits satisfying chosen parameters:
                                                olt Query

No. Score Match Length DB
                                                                                                                                                                                Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.
                                                                                                                                                                                                                                                                      Issued_Patents_AA:*

1: /cgn2_6/ptodata/1/iaa/5A_COMB.pep:*

2: /cgn2_6/ptodata/1/iaa/5B_COMB.pep:*

3: /cgn2_6/ptodata/1/iaa/6A_COMB.pep:*

4: /cgn2_6/ptodata/1/iaa/6B_COMB.pep:*

5: /cgn2_6/ptodata/1/iaa/PCTUS_COMB.pep:*

6: /cgn2_6/ptodata/1/iaa/backfiles1.pep:*
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        328717 seqs, 42310858 residues
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      BLOSUM62
Gapop 10.0 , Gapext 0.5
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 July 28, 2003, 15:40:06 ; Search time 30 Seconds (without alignments) 702.360 Million cell updates/sec
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          US-10-060-521-2
2540
1 MSKIELKQLSFAYDNQEVLL.....IEHDAHFMKKITDKKIVLKS 498
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  GenCore version 5.1.6 Copyright (c) 1993 - 2003 Compugen Ltd.
                                                                   Ħ
                                                                                                                                       SUMMARIES
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  0
                                                                 Description
```

Search completed: July 28, 2003, 15:50:53 Job time : 30 secs

```
OM protein - protein search, using sw model
                                                                                            GenCore version 5.1.6 Copyright (c) 1993 - 2003 Compugen Ltd.
```

July 28, 2003, 15:38:06 ; Search time 53 Seconds (without alignments) 1115.894 Million cell updates/sec

Title: Perfect score: US-10-060-521-2 2540

1 MSKIELKQLSFAYDNQEVLL.....IEHDAHFMKKITDKKIVLKS 498

Scoring table: BLOSUM62 Gapop 10.0 , Gapext 0.5

al number of hits satisfying chosen parameters:

0

451899 seqs, 118759770 residues

Searched:

Minimum DB seq length: 0 Maximum DB seq length: 2000000000

Post-processing: Minimum Match 75%

Maximum Match 100%

Listing first 1000 summaries

Database : Published Applications AA:*

1: /cgn2_6/prodata/2/pubpaa/US07_PUBCOMB.pep:*

2: /cgn2_6/prodata/2/pubpaa/JCT_NEW_PUB.pep:*

3: /cgn2_6/prodata/2/pubpaa/US06_NEW_PUB.pep:*

4: /cgn2_6/prodata/2/pubpaa/US06_PUBCOMB.pep:*

5: /cgn2_6/prodata/2/pubpaa/US06_PUBCOMB.pep:*

6: /cgn2_6/prodata/2/pubpaa/US08_NEW_PUB.pep:*

7: /cgn2_6/prodata/2/pubpaa/US08_NEW_PUB.pep:*

8: /cgn2_6/prodata/2/pubpaa/US08_PUBCOMB.pep:*

9: /cgn2_6/prodata/2/pubpaa/US09B_PUBCOMB.pep:*

10: /cgn2_6/prodata/2/pubpaa/US09B_PUBCOMB.pep:*

11: /cgn2_6/prodata/2/pubpaa/US09C_PUBCOMB.pep:*

12: /cgn2_6/prodata/2/pubpaa/US09C_PUBCOMB.pep:*

13: /cgn2_6/prodata/2/pubpaa/US09C_PUBCOMB.pep:*

14: /cgn2_6/prodata/2/pubpaa/US09C_PUBCOMB.pep:*

15: /cgn2_6/prodata/2/pubpaa/US09C_PUBCOMB.pep:*

16: /cgn2_6/prodata/2/pubpaa/US10B_PUBCOMB.pep:*

16: /cgn2_6/prodata/2/pubpaa/US10B_PUBCOMB.pep:*

17: /cgn2_6/prodata/2/pubpaa/US10B_PUBCOMB.pep:*

16: /cgn2_6/prodata/2/pubpaa/US10S_PUBCOMB.pep:*

17: /cgn2_6/prodata/2/pubpaa/US10S_PUBCOMB.pep:*

18: /cgn2_6/prodata/2/pubpaa/US10S_PUBCOMB.pep:*

18: /cgn2_6/prodata/2/pubpaa/US10S_PUBCOMB.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Regult No. Query Score Match Length DB ij Description

No matches found

Search completed: July 28, 2003, 15:48:26 Job time : 53 secs

```
GenCore version 5.1.6
Copyright (c) 1993 - 2003 Compugen Ltd.
```

OM protein - protein search, using sw model

July 28, 2003, 15:36:25; Search time 52 Seconds (without alignments) 921.000 Million cell updates/sec

Run on:

Title: Perfect score: Sequence:

US-10-060-521-2
2540
1 MSKIELKQLSFAYDNQEVLL.....IEHDAHFMKKITDKKIVLKS 498

Scoring table:

BLOSUM62 Gapop 10.0 , Gapext 0.5

Searched: 283308 seqs, 96168682 residues

al number of hits satisfying chosen parameters:

0

Minimum DB seq length: 0
Maximum DB seq length: 200000000

Post-processing: Minimum Match 75%

Maximum Match 100%

Listing first 1000 summaries

PIR_76:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Database :

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.

Query
Score Match Length DB Ħ

Description

No matches found

ch completed: July 28, 2003, 15:40:58 time : 52 secs

GenCore version 5.1.6 Copyright (c) 1993 - 2003 Compugen Ltd.

OM protein - protein search, using sw model

Run on:

July 28, 2003, 15:35:01; Search time 25 Seconds (without alignments) 936.772 Million cell updates/sec

Title: Perfect score: Sequence:

US-10-060-521-2 2540 1 MSKIELKQLSPAYDNQEVLL.....IEHDAHFMKKITDKKIVLKS 498

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 127863 seqs, 47026705 residues

al number of hits satisfying chosen parameters:

0

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 75%

Maximum Match 100%

Listing first 1000 summaries

Database :

SwissProt_41:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No. Query Score Match Length DB

ID

Description

No matches found

Search completed: July 28, 2003, 15:38:21 Job time: 33 secs

GenCore version 5.1.6 Copyright (c) 1993 - 2003 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 28, 2003, 15:38:26 ; Search time 103 Seconds (without alignments) 1247.672 Million cell updates/sec

Title: Perfect score:

BLOSUM62 Gapop 10.0 , Gapext 0.5

Sequence: US-10-060-521-2
2540
1 MSKIELKQLSFAYDNQEVLL.....IEHDAHFMKKITDKKIVLKS 498

Scoring table:

Searched: 830525 seqs, 258052604 residues

al number of hits satisfying chosen parameters:

0

Minimum DB seq length: 0 Maximum DB seq length: 200000000

Post-processing: Minimum Match 75%
Maximum Match 100%
Listing first 1000

summaries

Database :

SPTREMBL 23:*

1: sp_archea:*

2: sp_bacteria:*

3: sp_fungi:*

4: sp_human:*

5: sp_invertebrate

6: sp_manmal:*

7: sp_mclas:*

8: sp_organelle:*

9: sp_phage:*

10: sp_pdant:*

11: sp_virus:*

12: sp_virus:*

13: sp_unclassifie

14: sp_unclassifie

15: sp_rvirus:* sp_invertebrate:*
sp_mammal:*
sp_mhc:*

sp_organelle:*
sp_phage:*
sp_plant:*
sp_plant:*
sp_virus:*
sp_vertebrate:*
sp_unclassified:*
sp_rvirus:*
sp_bacteriap:*
sp_archeap:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No. Query Score Match Length DB ij Description

Search completed: July 28, 2003, 15:50:22 Job time : 110 secs

No matches found